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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/005,169	12/04/2001	Catherine Guenther	R-687	6876

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EXAMINER
BERTOGLIO, VALARIE E

ART UNIT	PAPER NUMBER
1632	10

DATE MAILED: 09/09/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/005,169	GUENTHER ET AL.	
	Examiner	Art Unit	
	Valarie Bertoglio	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 June 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,8-13,16,17 and 20-28* is/are pending in the application.

4a) Of the above claim(s) *1-4,11-13,16,17 and 20-26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8-10,27 and 28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicant's amendment filed on 06/23/2003 has been entered. Claims 5-7, 14-15 and 18-19 have been canceled. Claims 8-10 have been amended. Claims 27 and 28 have been added. Claims 1-4,8-13,16,17 and 20-28 are pending and claims 8-10, 27 and 28 are under consideration in the instant action.

Election/Restrictions

Claims 1-4,11-13,16,17 and 20-26 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 7.

Specification

The objection to specification on page 9 of the previous office action mailed 12/18/2002 is withdrawn in light of Applicants' amendment.

Claim Rejections - 35 USC § 101/112

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 8-10, 27 and 28 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility.

The claims are directed to a transgenic mouse whose genome comprises a disruption in a target gene, wherein the target gene is capable of homologous recombination with a nucleotide sequence homologous to SEQ ID NO: 1, and wherein the mouse exhibits impaired balance or motor coordination, or an increased or enhanced pain threshold. The claims are further directed to cells isolated from the same mouse.

The instant specification has contemplated that the nucleotide sequence set forth in SEQ ID NO: 1 encodes a nuclear hormone receptor. The instant specification has further contemplated that disruption of the nucleotide sequence set forth in SEQ ID NO: 1 in a mouse will produce a phenotype associated with a disruption of the NOR1 gene. The instant specification has purported that such mice may be used to identify agents that modulate or ameliorate a phenotype associated with a disruption in SEQ ID NO: 1. See page 17, lines 17-27.

The specification has provided general assertions that the claimed transgenic mice may be used to identify agents that affect a phenotype related to the mice. As such, the asserted utility, for the transgenic mouse embraced by the claims, of screening agents that may affect a phenotype of said mouse as provided by the instant specification and encompassed by the claims, does not appear to be specific and substantial. The asserted utility does not appear specific and substantial to the skilled artisan since the evidence of record has not provided any suggestion of a correlation between a homozygous disruption of the NOR1 gene, impaired balance or motor coordination, or an increased or enhanced pain threshold, and any disease or disorder. Since the evidence of record has not provided a correlation between increased impaired balance or motor coordination, or an increased or enhanced pain threshold and any disease or disorder, the utility of identifying agents that affect impaired balance or motor coordination, or an increased or

enhanced pain threshold is not apparent. The evidence of record has not provided any other utilities for the transgenic mouse embraced by the claims that are specific, substantial, and specific and substantial.

The instant specification has disclosed a transgenic mouse whose genome comprises a disruption in SEQ ID NO: 1, wherein the mouse exhibits impaired balance or motor coordination, or an increased or enhanced pain threshold. See page 48. The claims encompass said mouse and cells obtained from the mouse. The instant specification has discussed that the animals and cells of the instant invention can be used as models of disease (refer to pages 17-18). Specifically, the specification states that agents can be identified on the basis of their ability to affect at least one phenotype associated with a disruption of NOR1 (page 18, lines 10-12). However, the evidence of record, while contemplating that the phenotypes exhibited by the claimed transgenic mice are associated with disease does not provide a correlation between the phenotypes of the claimed mouse and any disease or disorder. Furthermore, neither the specification nor any art of record provides evidence of the existence of a correlation between the phenotypes displayed by the claimed mice and a disease or disorder, leaving the skilled artisan to speculate and investigate the uses of the transgenic mouse embraced by the claims. The specification essentially gives an invitation to experiment wherein the artisan is invited to elaborate a functional use for the transgenic mouse embraced by the claims. In light of the above, the skilled artisan would not find the asserted utility of the transgenic mouse embraced by the claims to be specific and substantial.

Claims 8-10, 27 and 28 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial

asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Upon overcoming the utility and enablement rejections set forth above, the following issue of enablement under 35 USC 112-1st paragraph must also be addressed.

The breadth of claims 8-10,27 and 28 is such that they encompass chimeric animals (genetic mosaics) wherein only a portion of the cells of the animal comprises the claimed genetic disruption. The specification teaches making transgenic animals whose genome comprises a homozygous disruption in the NOR1 gene in all somatic and germ cells wherein the transgenic mice display impaired balance or motor coordination, or an increased or enhanced pain response threshold. The specification does not teach a chimeric animal with these phenotypes. The method of making genetic mosaic animals is such that each resulting chimera is comprised of a different, unpredictable ratio of cells of various genotypes. This ratio cannot be predetermined. Furthermore, the spatial distribution of cells of each genotype cannot be predetermined. Therefore, the phenotype of chimeric animals is not only dependent upon the genotype of the cells (which is unpredictable as set forth by the state of the art outlined on pages 11-13 of the previous office action mailed 12/18/2002) but is also dependent upon the spatial distribution of the cells and their relative population size. Thus, the phenotype of the chimeric animals encompassed by the claims is highly unpredictable. It would require undue experimentation for one of skill in the art to determine how to overcome the unpredictability associated with making chimeric animals such that the proportion and population of cells harboring a genetic alteration could be controlled in such a way as to increase the predictability of the phenotype of the resulting chimeric animal.

The rejection of claims 8-10,14,15, 18 and 19 under 35 USC 112-1st paragraph for lacking enablement as set forth on pages 10-15 of the previous office action is withdrawn in view of Applicants' arguments.

The rejection of claims 5-9,14,15,18 and 19 under 35 USC 112-1st paragraph for lacking written description, as set forth on pages 9-10 of the previous office action is withdrawn in view of Applicants' arguments.

Claim Rejections - 35 USC § 112-2nd paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 8-10, 27 and 28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 8 and 10 refer to a homozygous disruption in NOR1. As written, the term "NOR1" can be interpreted as referring to the NOR1 gene or the NOR1 protein. A protein cannot have a homozygous disruption. Because the claim uses the phrase "homozygous disruption", the term "NOR1" can be clarified by changing it to "the NOR1 gene" in line 2 of claims 8 and 10 and line 4 of claim 10. Claims 9, 27 and 28 depend from claim 8 and are included in this rejection.

Claim 10 is unclear because the language of the preamble is directed to a genetic mosaic as it states "...a transgenic mouse comprising a homozygous disruption..." However, step (d) of the claim encompasses breeding the chimeric mouse to generate transgenic mice whose genome comprises a homozygous disruption in the NOR1 gene in all somatic and germ cells. Correction is required.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Valarie Bertoglio whose telephone number is 703-305-5469. The examiner can normally be reached on Mon-Weds 6:00-2:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds can be reached on 703-305-4051. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1234.

PETER PARAS
PATENT EXAMINER

Valarie Bertoglio
Examiner
Art Unit 1632